

Biological Soft X-ray Microscopy: The source

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Biological Soft X-ray Microscopists:

Why we are **really** happy new sources are being developed

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Why Biological Microscopy?

Why the pressing **need** for new sources?

What's in it for you?

A close-up, black and white portrait of Michael Douglas as Gordon Gekko, looking directly at the camera with a serious expression. He is wearing a dark suit and a white shirt.

MICHAEL DOUGLAS

CHARLIE SHEEN

DARYL HANNAH

AN OLIVER STONE FILM

Source Street

“Funding is good”

- Gordon Gekko Ph.D.

Funding for biology/biomedical research

- Pharmaceutical Industry \$160+ Billion per year
- NIH \$32 Billion per year
- Etc. etc.

GDP of Republic of Ireland \$294 Billion

Soft x-ray microscopy is generally applicable

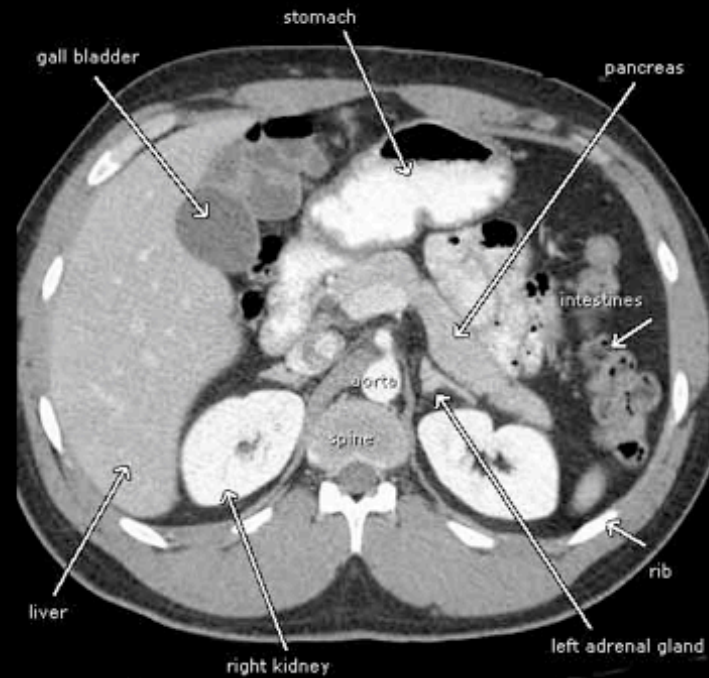
Soft X-ray Microscopy

- Images biological cells in 3D
 - High-resolution
 - No need to slice, stain, chemically fix, dehydrate specimen
-
- Similar in concept to medical CT scans

Computed Tomography (CT) for Clinical Diagnosis

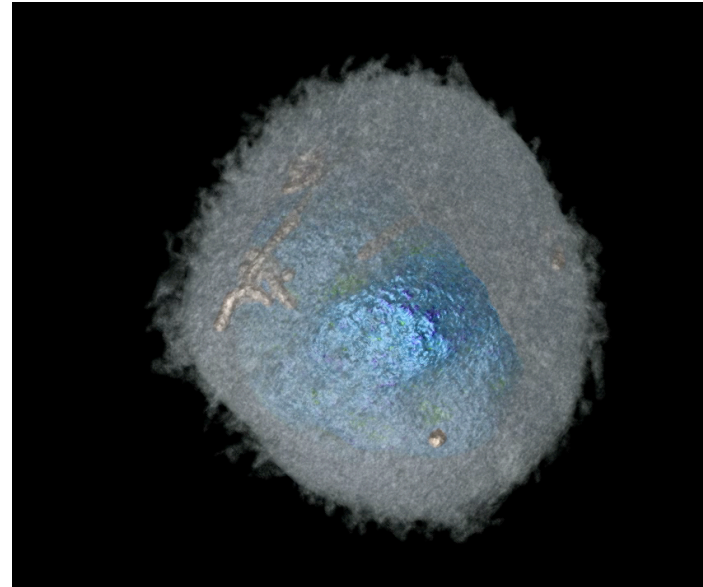
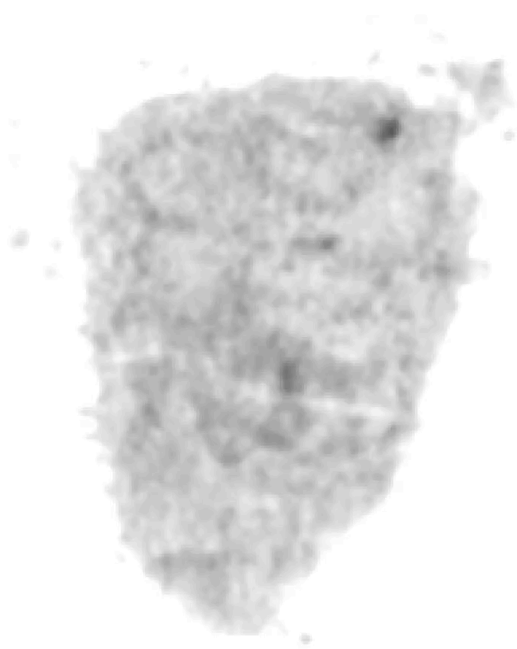







Courtesy of Wikipedia



**CT scan of abdomen:
Absorption contrast**

Soft x-ray CT of a single cell



-  Cytoplasm - grey
-  Heterochromatin - blue
-  Euchromatin - green
-  Mitochondria - bronze
-  Endoplasmic reticulum - red

Applications: Biological Soft X-ray Microscopy

- Testing candidate drugs *in cellulo*
- Optimizing Bio-manufacturing processes
- Identifying environmental hazards – nanotoxicology
- Understanding disease
- Etc.

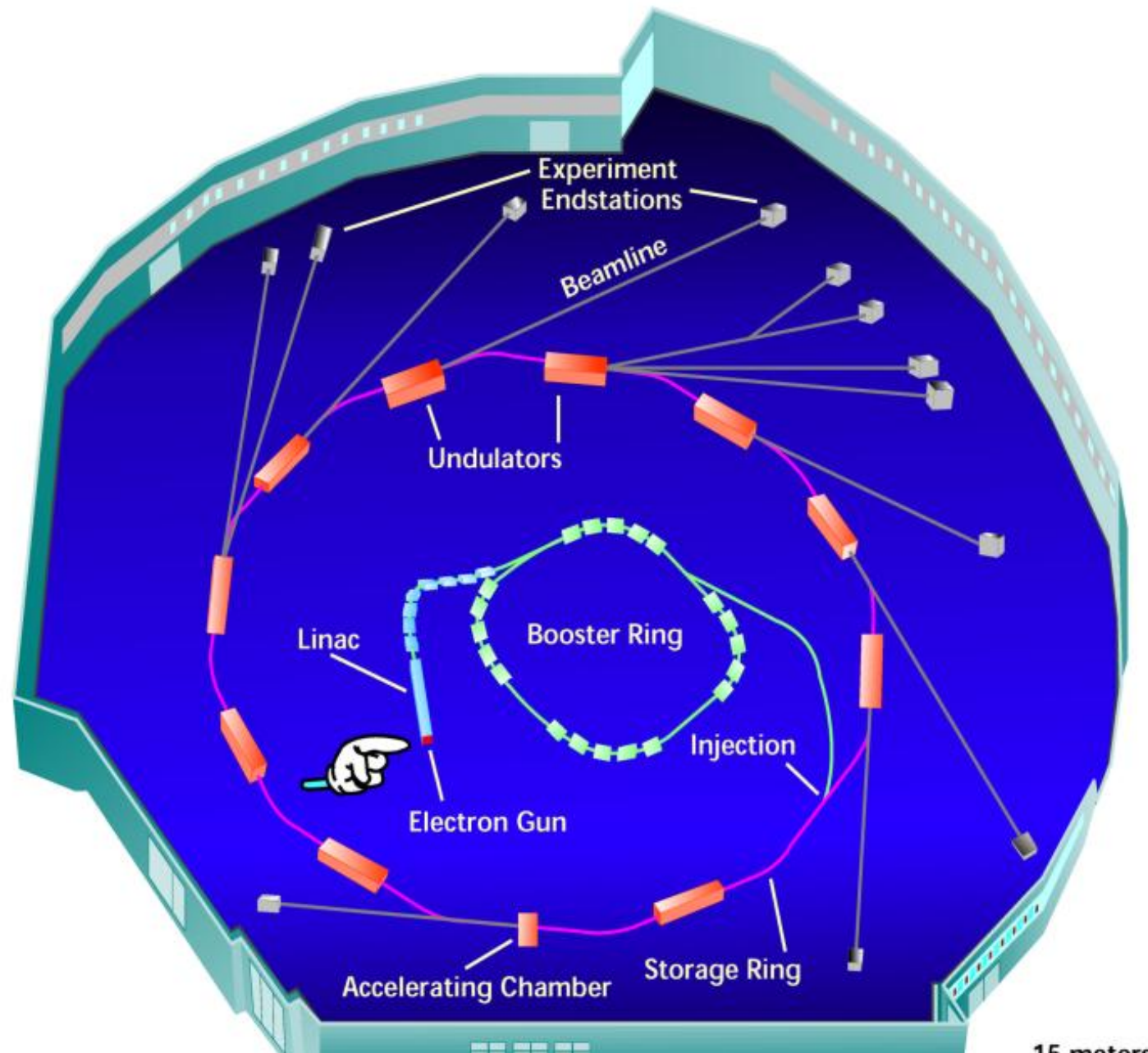
Growth of biological soft x-ray microscopy

limited by source availability

National Center for X-ray Tomography

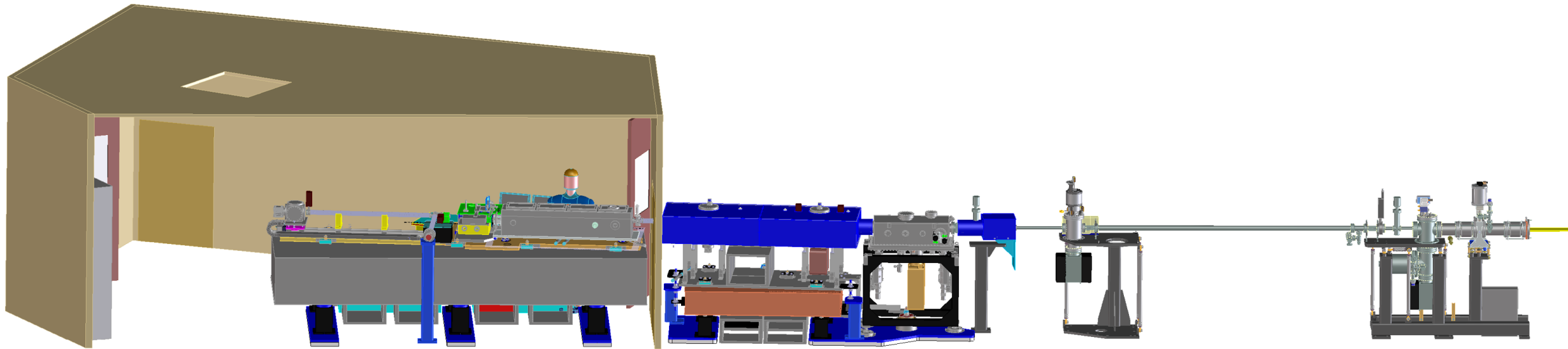
Designed, built and now operate a Soft X-ray Microscope for biology
at the Advanced Light Source, Berkeley

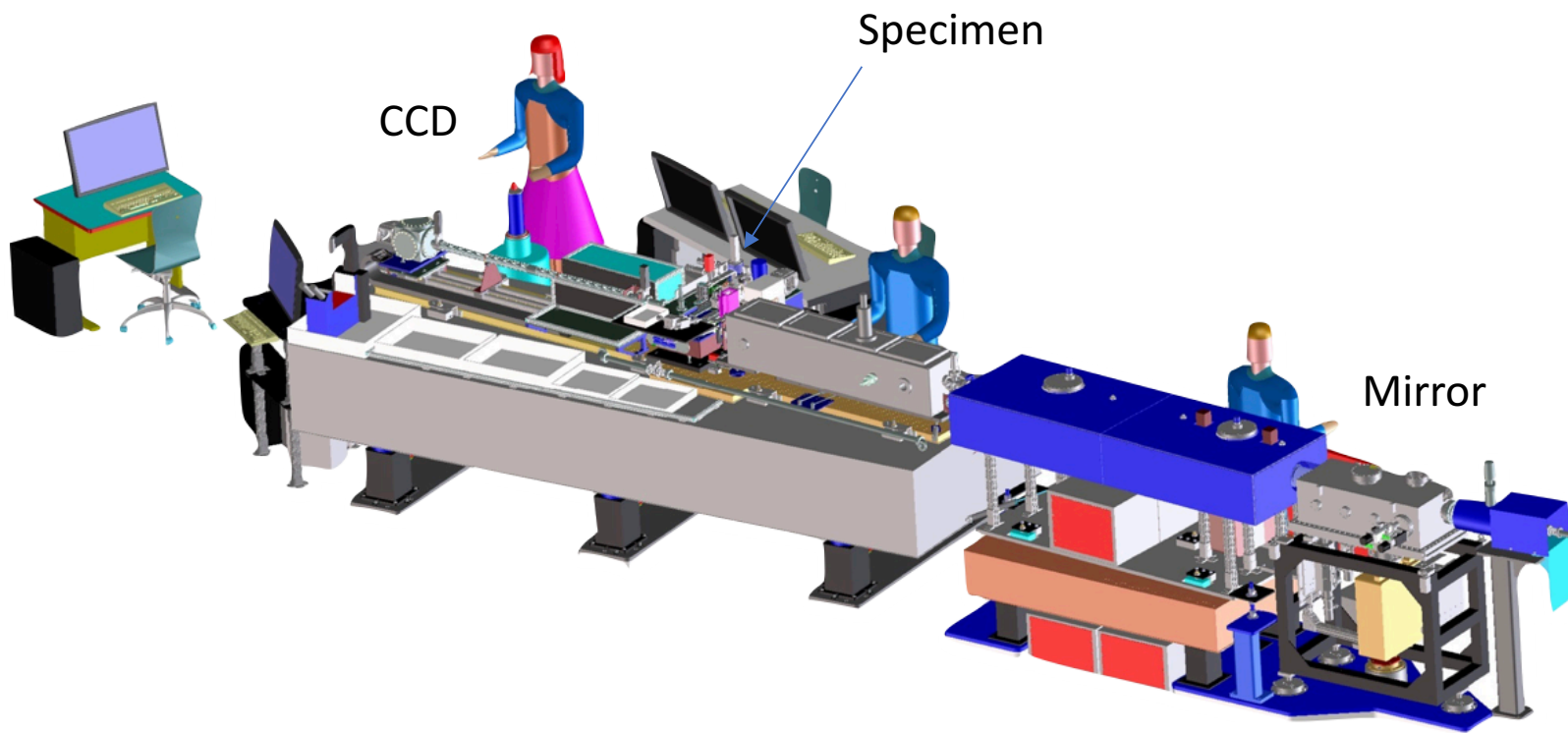




15 meters

NCXT Soft X-ray Microscope

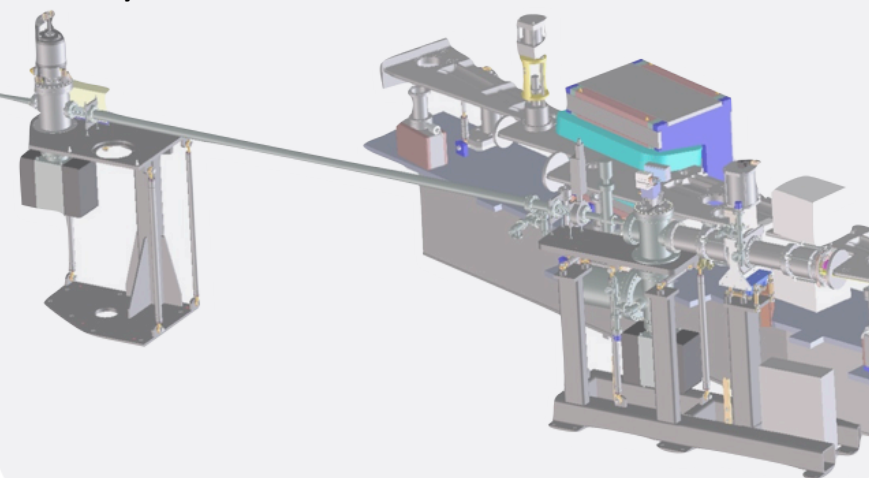


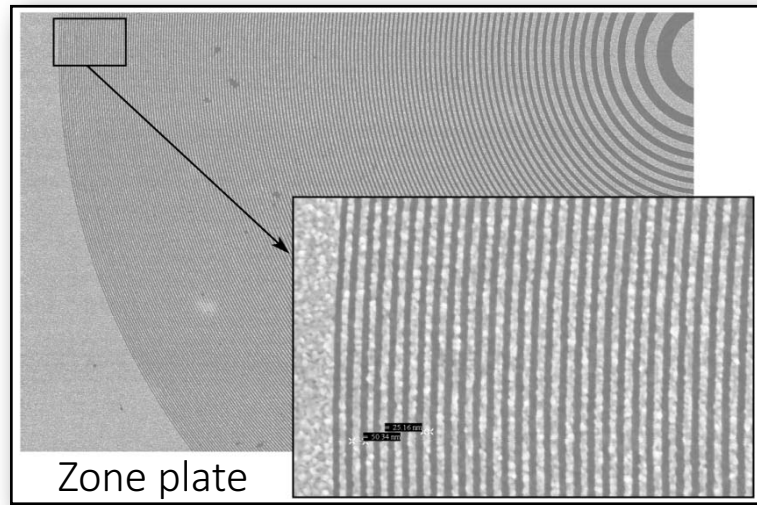


Behind concrete shield wall

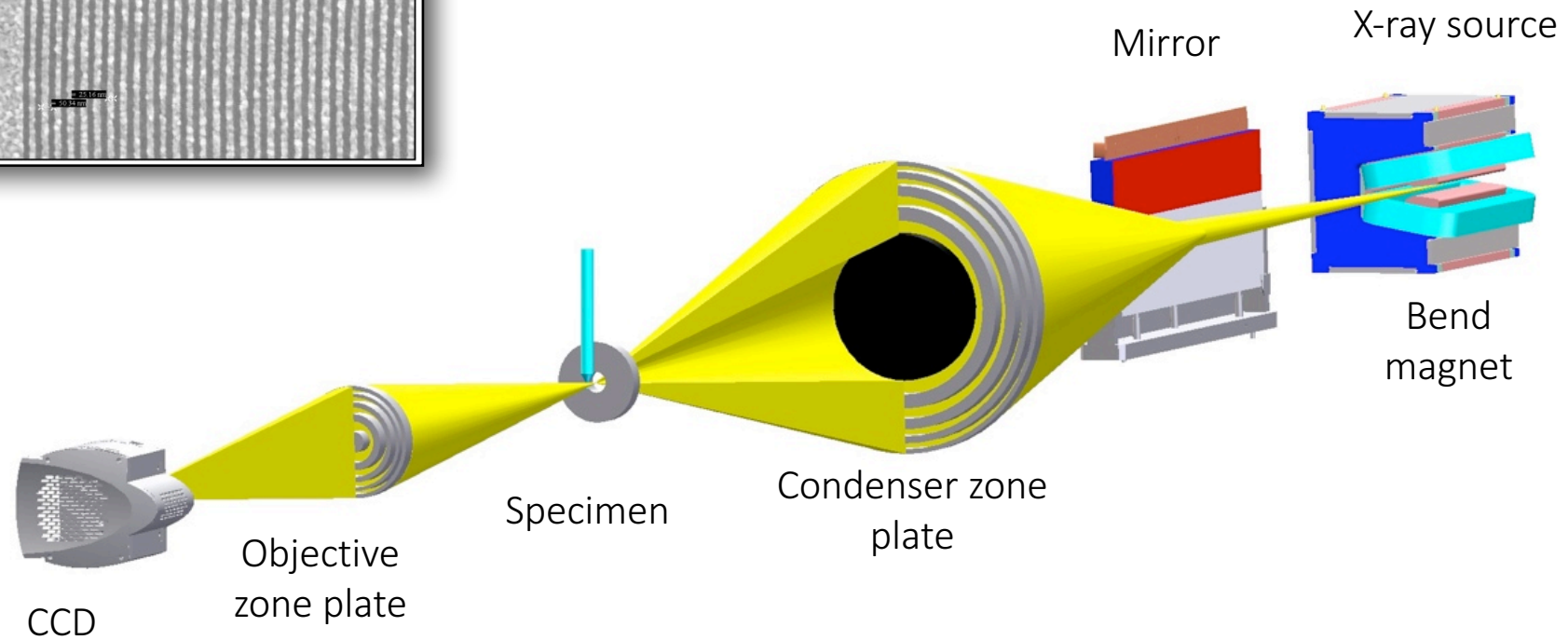
Personnel safety shutter

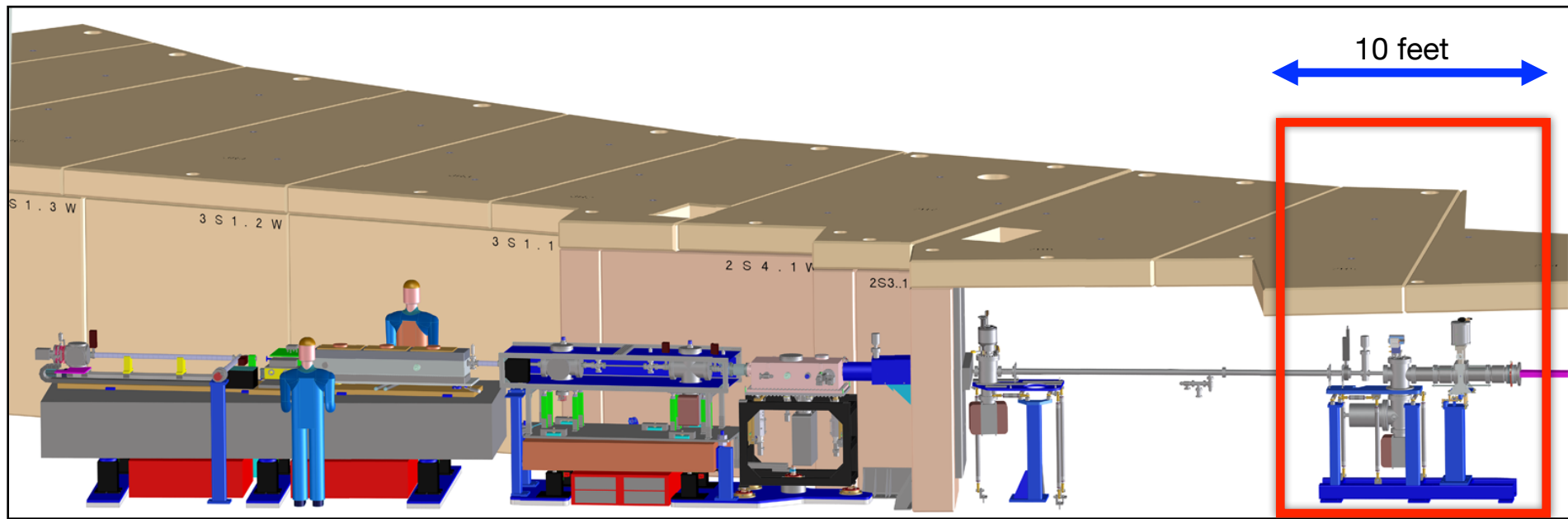
Bend magnet source



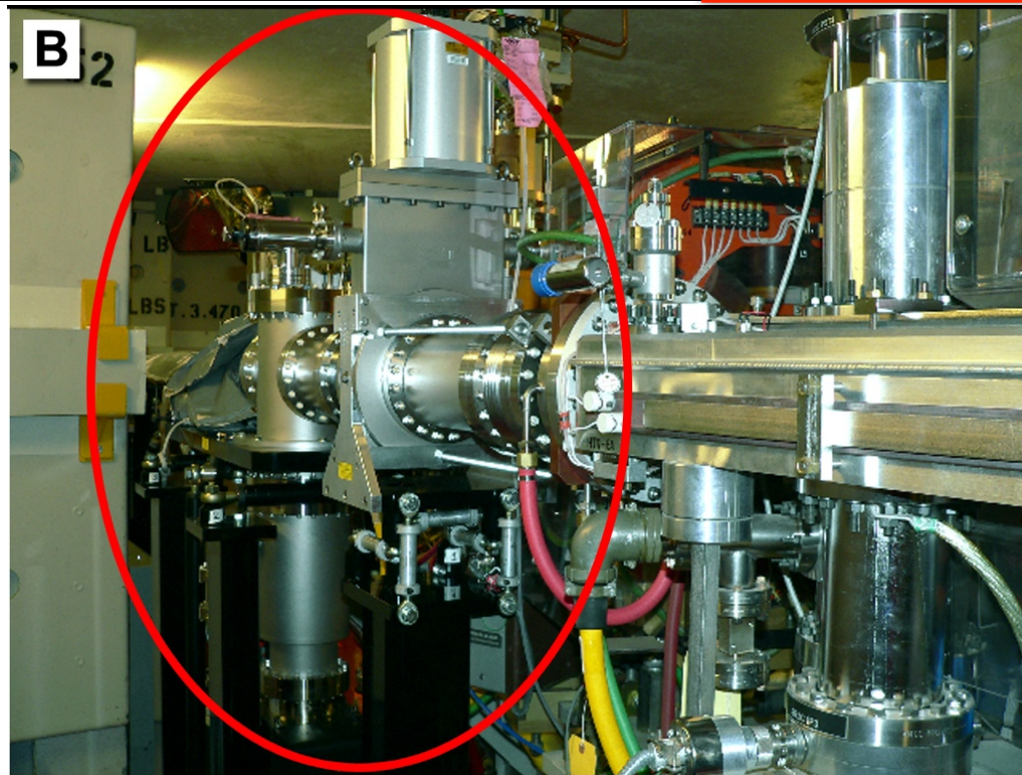
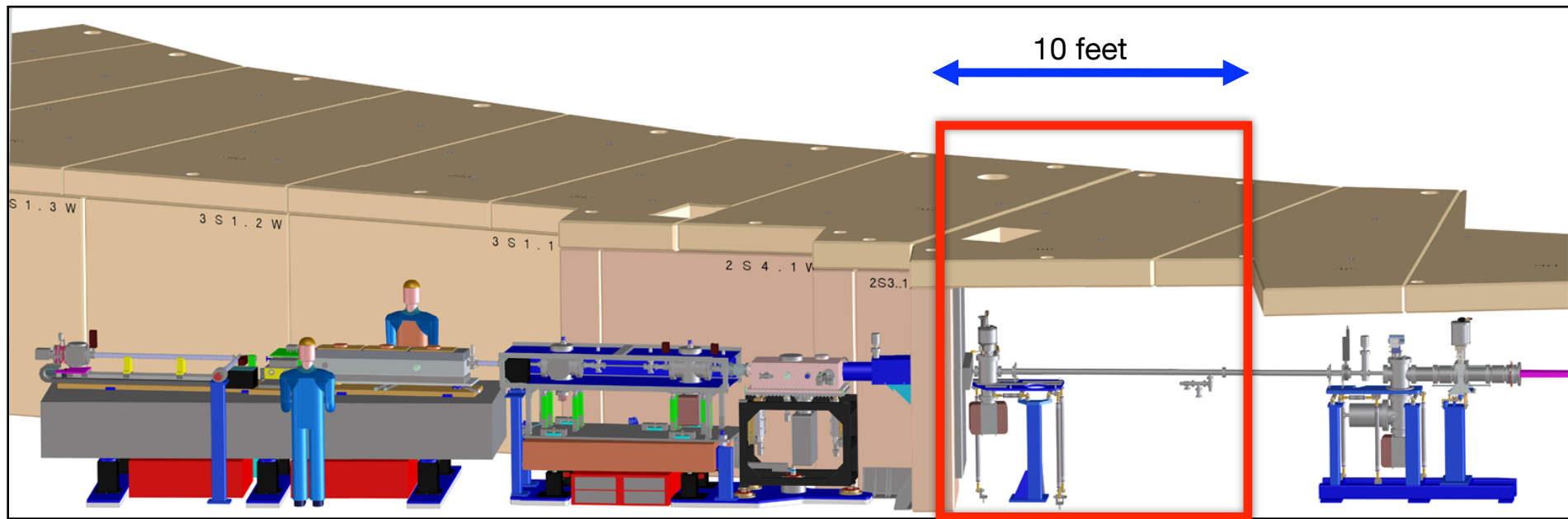


Full-field, Transmission Soft X-ray Microscope

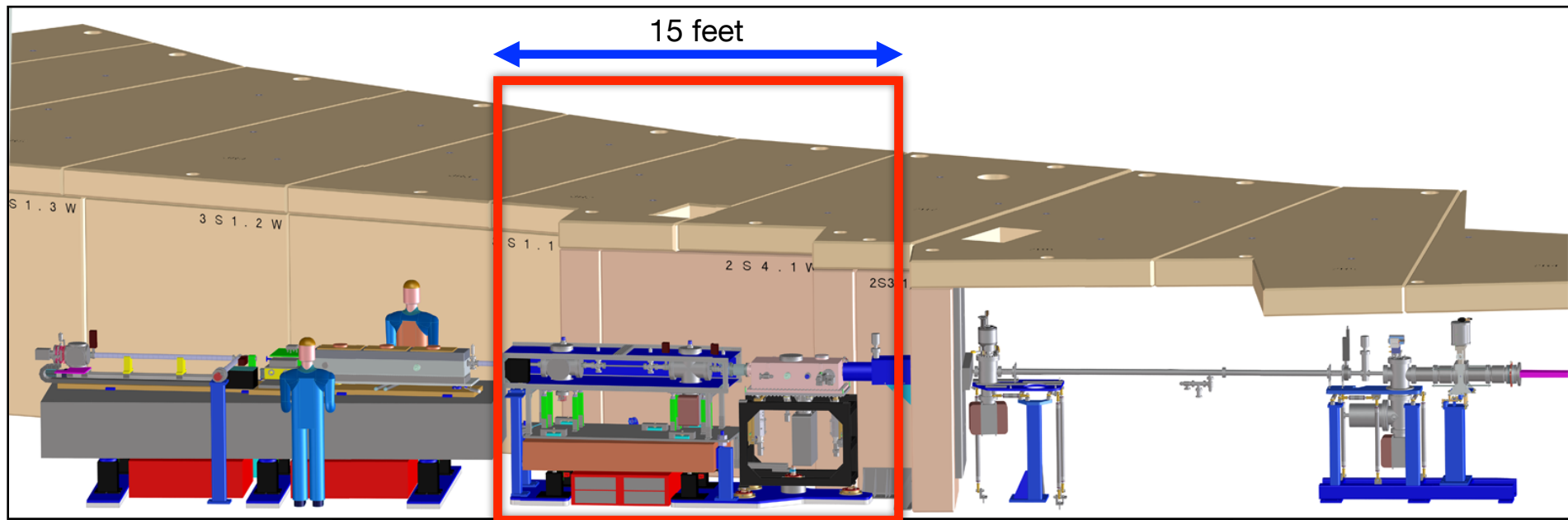




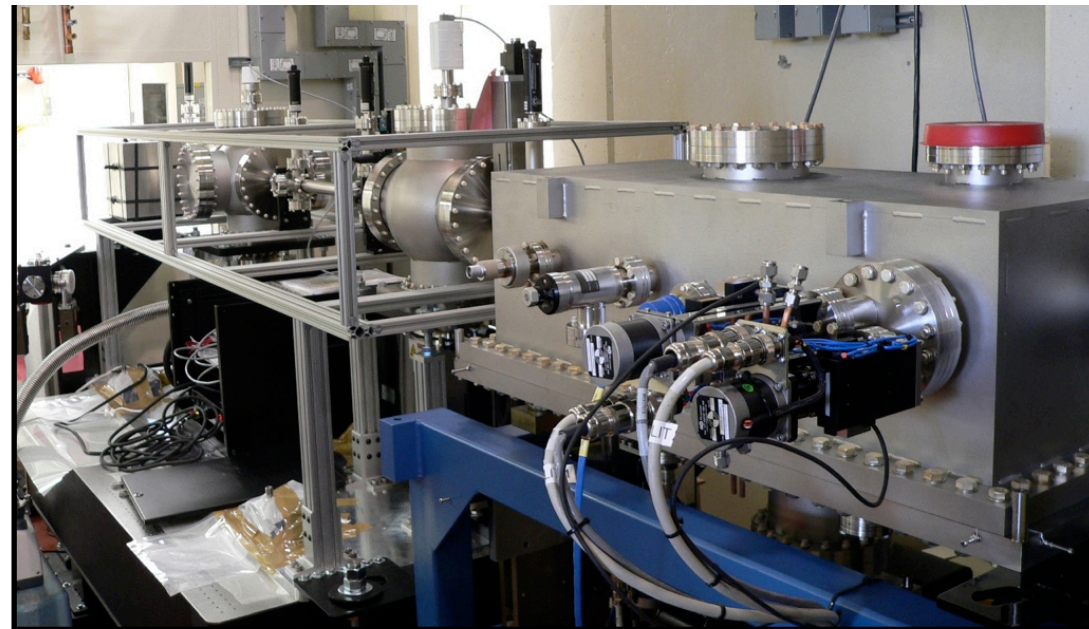
photon
shutter

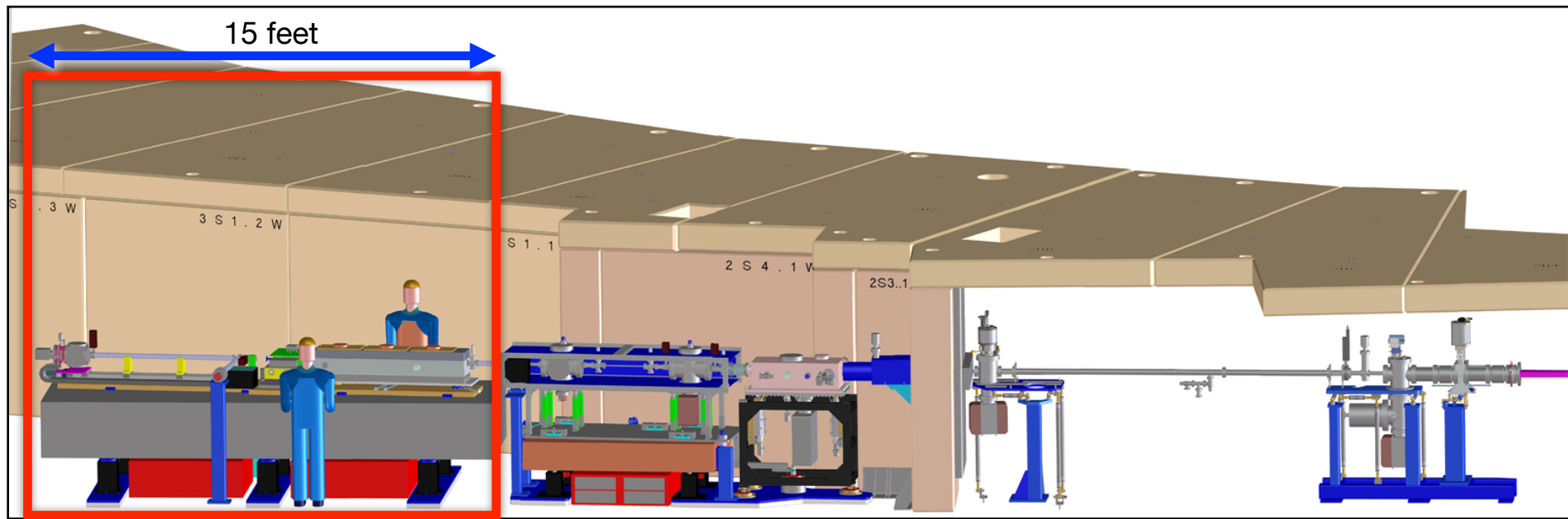


personnel
safety shutter



mirror and
branchline





experimental
station

XM2 specs

Source type: 1.3T Bend magnet

Mirror: Flat silicon; striped with nickel and gold surfaces

Monochromator: Zone-plate linear

Energy range (eV) 400–1300

Flux (512 eV): 5×10^7 photons $\text{s}^{-1} \mu\text{m}^{-2}$

Field of view: $15 \times 15 \mu\text{m}$

Detector: 2048 x 2048 back-thinned CCD; pixel size $13.5 \times 13.5 \mu\text{m}$

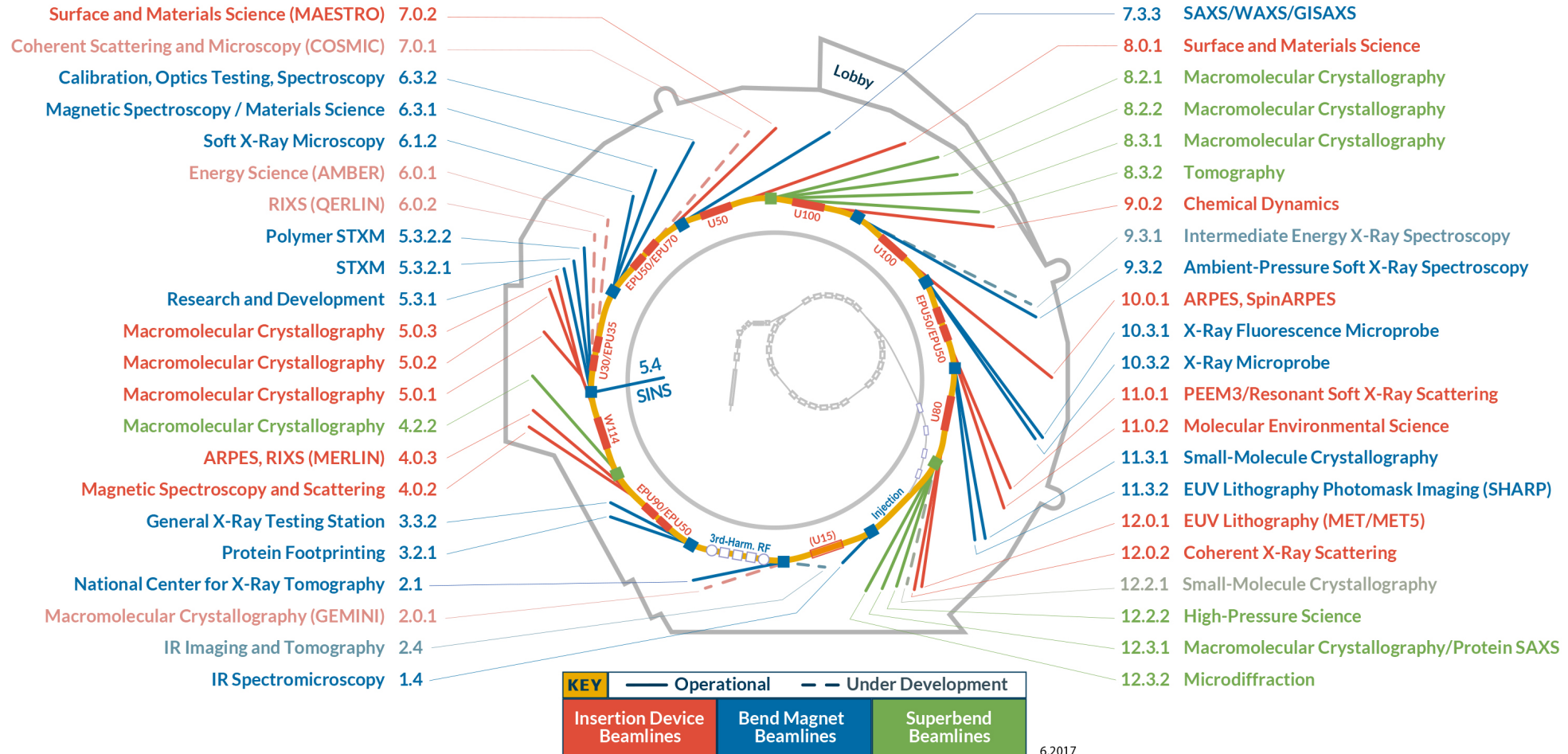
Le Gros, M.A., et al. Biological soft X-ray tomography on beamline 2.1 at the Advanced Light Source. *J Synchrotron Radiation*, (2014) **21**, 1370-7

Extremely expensive to build
microscope @synchrotron



Synchrotrons are already packed!

ALS Beamlines



Synchrotron-based microscopes

- Very expensive to build and operate
 - high overhead rates
 - bureaucratic burden
 - time spent getting funding

- Collaborators have to travel*
 - regular use becomes expensive
 - adds unknown factors to specimen prep

* Some don't mind spending winter months in California

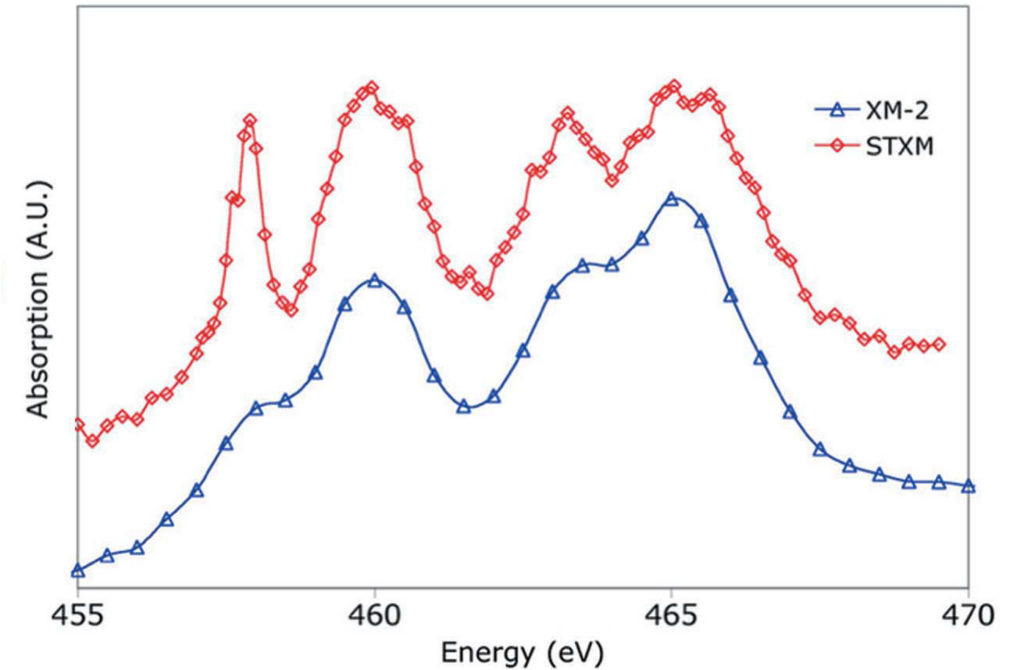
Advice

- Talk to biologists
- Biology is messy -- 'Good enough' is often better than 'the ultimate'

“Good enough” is better

Monochromaticity 300 ($E/\Delta E$)

Increased depth of field



Energy scan TiO₂ nanoparticles

Advice

- Talk to biologists
- Biology is messy -- 'Good enough' is often better than 'the ultimate'
- Exposure time of seconds is OK, milliseconds is luxury

Summary

Growth of biological soft x-ray microscopy is source limited

Large potential market for 'in-house' soft x-ray microscopes

- Pharmaceutical industry

- Biotech

- Academic research

New source just needs to be 'good enough'

- Doesn't need to equal a synchrotron

A photograph of the Golden Gate Bridge in San Francisco, taken from a distance across the water. The bridge is silhouetted against a bright orange sunset sky. The water is dark, and the surrounding hills are also silhouetted. The overall mood is serene and majestic.

National Center for X-ray Tomography

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